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*SPD RAL*

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/617,645 07/14/00 ARIYASU

T ARTYASU=1A

001444  
BROWDY AND NEIMARK, P.L.L.C.  
624 NINTH STREET, NW  
SUITE 300  
WASHINGTON DC 20001-5303

HM12/1109

EXAMINER

KAUFMAN, C

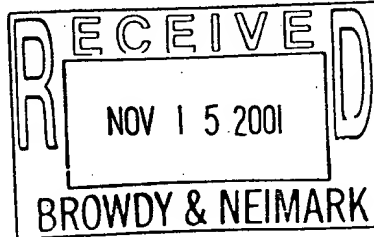
ART UNIT

PAPER NUMBER

1646

DATE MAILED:

11/09/01



Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

DOCKETED

*Amend = 9FE 2002*

# Office Action Summary

Application No.

09/617,545

Applicant(s)

ARIYASU ET AL.

Examiner

Claire M. Kaufman

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 8-10, 15 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 11-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-16 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 July 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/063,778.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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**DETAILED ACTION**

The amendment filed 9/10/01 has been entered.

***Election/Restrictions***

Applicant's election with traverse of Group I in Paper No. 5 is acknowledged. The traversal is on the ground(s) that examination of plural groups would not involve a serious burden because there is not a serious burden to examine a plurality of groups and one cannot completely search Group I without searching Group II. This is not found persuasive because a search for the full-length encoding nucleic acid is not required for a search of the invention of Group II. The recombinant method producing the encoded protein Group I (*i.e.*, the antigen) does not require searching for anticipatory art for the protein itself, which is not true for the antibody search. Additionally, as previously stated, the different classifications support the need for different searches for each group. Further, the fact that the antibody of Group II may bind to proteins other than human Desert hedgehog, *e.g.*, Sonic hedgehog--see claim 9, means that the search for the antibody requires searches of proteins and/or encoding nucleic acids in addition to human Desert hedgehog, which searches are not required for the DNA claimed. For these reasons, the inventions are distinct.

The requirement is still deemed proper and is therefore made FINAL.

***Specification***

Applicants are required to use the heading "Brief Description of the Drawings" instead of "Brief Description of the Accompanying Drawings" at page 4. See MPEP 608.01(f).

The disclosure is objected to because of the following informalities: On page 4, fourth line in the paragraph beginning "In FIG. 1," "*coli*;t he" should be ""*coli*; the" .

Appropriate correction is required.

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***Claim Objections***

Claims 5 and 14 are objected to because of the following informalities: in line 2 of claim 5, "ore" should be ~~more~~; in the last line of claim 14, "Desert" should not be capitalized to be consistent with the rest of the claims. Appropriate correction is required.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Since the claimed DNA is naturally occurring and is not claimed as purified and/or isolated, the claims do not show the hand of man involved in the invention and, therefore, are unpatentable. See MPEP § 706.03(a) and 2105.

***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 11, 12, 14 and claims 2-7 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting an essential step, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: the expression of the DNA. "Allowing" expression does not mean that expression occurs, only that it can occur. "The generated hedgehog protein" is not required to be the one encoded by the DNA which encodes a desert hedgehog protein of human origin. It can instead be an endogenous hedgehog protein, depending on the cell type used.

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Claim 12 is indefinite because it is unclear what a "transformant" is. The specification describes host cells transfected with DNA but is not clear that a "transformant" is limited to a host cell comprising heterologous DNA introduced by transfection or transformation. The claim could be clarified by using phrasing such as "wherein said DNA is expressed through culturing of a host cell transformed by introduction of said DNA which encodes a desert hedgehog protein of human origin".

Claim 12 is also indefinite because 1) it is not clear that the DNA of the last line encodes a human Desert hedgehog protein. If it does not, then there is a gap in steps between making the HuDhh DNA capable of being expressed and getting expression when the DNA expressed encodes a different hedgehog protein. 2) It is not clear which DNA "the DNA" in line 1 is. That is, it is not clear it is said DNA that encodes a desert hedgehog protein of human origin.

Claims 1, 11 and 14 are indefinite because it is unclear what distinguishes a desert hedgehog (Dhh) protein from other proteins, particularly other hedgehog proteins. As a result, the metes and bounds of the claims is not clear. There are no characteristics by which one could distinguish the DNA encoding a Dhh protein of the instant invention from other encoding DNAs. Note that claims 2-4 require only that it contain a part of a specified amino acid sequence. Since a part can be one nucleotide, almost all DNAs comprise at least one nucleotide in common with the sequences listed. For these reasons, the metes and bounds of the claims cannot be determined.

Claim 5 is indefinite because since there is no specified DNA sequence for the DNA of claim 1, one cannot know if the DNA of claim 5 is a different degenerate sequence.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 11-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA comprising SEQ ID NO:5 or 6 or encodes a

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protein comprising the sequence of SEQ ID NO:2 or 3 (*i.e.*, a degenerate DNA), does not reasonably provide enablement for a DNA that is not one of the above but which must still encode a hedgehog or desert hedgehog protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification teaches DNA encoding a mature and full-length form (SEQ ID NO: 5 and 6, respectively) of the human desert hedgehog protein of SEQ ID NO:2 and 3. Also taught are partial encoding DNA sequences (SEQ ID NO:4, 8-10) and primers used for PCR amplification, with SEQ ID NO:4 encoding a fragment of the mature protein and SEQ ID NO:8-10 encoding part of a HuDhh precursor (p. 33, middle). The mature mouse Dhh sequence is 374 amino acids long and over 97% identical to SEQ ID NO:2 of the instant application (Ingham et al., US Patent 5,789,543, see attached "COMPARISON"). Human Dhh of SEQ ID NO:2 is 374 amino acids long. SEQ ID NO:1, encoded by SEQ ID NO:4, is 176 amino acids long. The claims have no functional limitation to allow one skilled in the art to identify the claimed subject matter by anything but sequence relationship or name, which gives great breadth to the claims.

There is no disclosure of a function of the claimed HuDhh. There is no guidance for making a DNA without knowing what it looks like or what it does. The specification does not provide limitations on what portion(s) of a DNA must be the same as SEQ ID NO:5 or what minimum shared sequence identity must be present for DNA to be considered an HuDhh-encoding polynucleotide. Note that the language "contains a part or the whole of ... SEQ ID NO:5" (claim 3), does not provide a structural limitation since a part can be one nucleotide. Because the hh family has not only Dhh but also Shh and Ihh, which share sequence identity and have some shared functions like binding patched receptor, it is not straight forward to say that a protein is a Dhh if there is no structure to distinguish it from a Shh or Ihh protein and a function specific to Dhh and not the other proteins of the hh family. If the DNA cannot be used as a probe which will specifically identify other Dhh-encoding polynucleotides with the exclusion of other hh-encoding polynucleotides and the DNA cannot be used to encode a protein which the skilled artisan could use without undue experimentation, then one would not know how to use the claimed DNA. For these reasons, it would require undue experimentation to practice the claimed invention.

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***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Drummond et al. (GenBank Accession No. U59748, also known as BC, cited by Applicants).

Drummond (GenBank Accession No. U59748) teaches part of the nucleic acid encoding human Dhh and the corresponding deduced amino acid sequence. The sequence isolated was mRNA, but that shown is DNA. This nucleic acid encodes a human Dhh protein, though not the full-length or mature form of SEQ ID NO:2 or 3 taught in the instant application. Note that the neither the claims nor the specification have a limitation that the Dhh protein of the instant specification must encode a full-length or functional protein.

***Prior Art***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Epstein et al. (C, US Patent 5,759,811) describe a single mutation in human Shh associated with tumorigenicity, the existence of a partial nucleic acid sequence of human Dhh and the desire to test hedgehog proteins besides Shh for the ability to promote tumor growth. Ingham et al. (B, US Patent 5,844,079) teach mouse Desert hedgehog (Dhh, SEQ ID NO:9), mouse and human Indian hedgehog (Ihh, SEQ ID NO: 14 and 10, respectively), and mouse, chicken, human and zebrafish Sonic hedgehog (Shh, SEQ ID NO: 11, 8, 13 and 12, respectively). Ingham et al. (US Patent 5,789,543) teaches mouse Dhh (SEQ ID NO:4). No full-length DNA encoding a Dhh protein of human origin appears in the prior art.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

November 7, 2001



; Patent No. 5789543: COMPARISON TO SEQ ID NO:2

; APPLICANT: Ingham, Phillip W.

APPLICANT: McMahon, Andrew P.

APPLICANT: Tabin, Clifford J.

7 TITLE OF INVENTION: Vertebrate Embryonic Pattern-Inducing

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## ; CURRENT APPLICATION DATA:

APPLICATION NUMBER: US/08/176,427B

FILING DATE: 30-DEC-1993

; INFORMATION FOR SEQ ID NO: 4:

## ; SEQUENCE CHARACTERISTICS:

; LENGTH: 396 amino acids

; TYPE: amino acid

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;      TOPOLOGY:  linear

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; MOLECULE TYPE: protein

Query Match 97.6%; Score 1761; DB 2; Length 396;  
Best Local Similarity 97.3%; Pred. No. 1.9e-191;  
Matches 364; Conservative 9; Mismatches 1; Indels 0; Gaps 0;

QY      1 CGPGRGPVGRRRYARKQLVPLLYKQFVPGVPERTLGASGPAEGRVARGSERFRDLVPNYN 60  
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Db     23 CGPGRGPVGRRRYVRKQLVPLLYKQFVPSMPERTLGASGPAEGRVTRGSEFRDLVPNYN 82

Qy 61 PDIIFKDEENSGADRLMTERCKERVNALAIAMNMWPGVRLRVTEGWDEDGHHAQDSLHY 120  
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 Db 83 PDIIFKDEENSGADRLMTERCKERVNALAIAMNMWPGVRLRVTEGWDEDGHHAQDSLHY 142

QY 121 EGRALDITTSDRDRNKYGLLARLAVEAGFDWVYYESRNHIHVSVKADNSLAVRAGGCFPG 180  
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |  
Db 143 EGRALDITTSDRDRNKYGLLARLAVEAGFDWVYYESRNHIHVSVKADNSLAVRAGGCFPG 202

QY 181 NATVRLWSGERKGLRELHRGDWVLTDASGRVVPTPVLLFLDRDLQRRASFVAVETEWPP 240  
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Db 203 NATVRLRSGERKGLRELHRGDWVLAADAAGRNVPTPVLLFLDRDLQRRASFVAVETERPP 262

QY 241 RKLLLT<sup>241</sup> PWHLVFAARGPAPAPGDFAPVFARRLRAGDSVLAPGGDALRPARVARVAREEAV 300  
 |||||<sup>242</sup> |||||<sup>243</sup> |||||<sup>244</sup> |||||<sup>245</sup> |||||<sup>246</sup> |||||<sup>247</sup> |||||<sup>248</sup> |||||<sup>249</sup> |||||<sup>250</sup> |||||<sup>251</sup> |||||<sup>252</sup> |||||<sup>253</sup> |||||<sup>254</sup> |||||<sup>255</sup> |||||<sup>256</sup> |||||<sup>257</sup> |||||<sup>258</sup> |||||<sup>259</sup> |||||<sup>260</sup> |||||<sup>261</sup> |||||<sup>262</sup> |||||<sup>263</sup> |||||<sup>264</sup> |||||<sup>265</sup> |||||<sup>266</sup> |||||<sup>267</sup> |||||<sup>268</sup> |||||<sup>269</sup> |||||<sup>270</sup> |||||<sup>271</sup> |||||<sup>272</sup> |||||<sup>273</sup> |||||<sup>274</sup> |||||<sup>275</sup> |||||<sup>276</sup> |||||<sup>277</sup> |||||<sup>278</sup> |||||<sup>279</sup> |||||<sup>280</sup> |||||<sup>281</sup> |||||<sup>282</sup> |||||<sup>283</sup> |||||<sup>284</sup> |||||<sup>285</sup> |||||<sup>286</sup> |||||<sup>287</sup> |||||<sup>288</sup> |||||<sup>289</sup> |||||<sup>290</sup> |||||<sup>291</sup> |||||<sup>292</sup> |||||<sup>293</sup> |||||<sup>294</sup> |||||<sup>295</sup> |||||<sup>296</sup> |||||<sup>297</sup> |||||<sup>298</sup> |||||<sup>299</sup> |||||<sup>300</sup> |||||<sup>301</sup> |||||<sup>302</sup> |||||<sup>303</sup> |||||<sup>304</sup> |||||<sup>305</sup> |||||<sup>306</sup> |||||<sup>307</sup> |||||<sup>308</sup> |||||<sup>309</sup> |||||<sup>310</sup> |||||<sup>311</sup> |||||<sup>312</sup> |||||<sup>313</sup> |||||<sup>314</sup> |||||<sup>315</sup> |||||<sup>316</sup> |||||<sup>317</sup> |||||<sup>318</sup> |||||<sup>319</sup> |||||<sup>320</sup> |||||<sup>321</sup> |||||<sup>322</sup> |||||<sup>323</sup> |||||<sup>324</sup> |||||<sup>325</sup> |||||<sup>326</sup> |||||<sup>327</sup> |||||<sup>328</sup> |||||<sup>329</sup> |||||<sup>330</sup> |||||<sup>331</sup> |||||<sup>332</sup> |||||<sup>333</sup> |||||<sup>334</sup> |||||<sup>335</sup> |||||<sup>336</sup> |||||<sup>337</sup> |||||<sup>338</sup> |||||<sup>339</sup> |||||<sup>340</sup> |||||<sup>341</sup> 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|||||<sup>542</sup> |||||<sup>543</sup> |||||<sup>544</sup> |||||<sup>545</sup> |||||<sup>546</sup> |||||<sup>547</sup> |||||<sup>548</sup> |||||<sup>549</sup> |||||<sup>550</sup> |||||<sup>551</sup> |||||<sup>552</sup> |||||<sup>553</sup> |||||<sup>554</sup> |||||<sup>555</sup> |||||<sup>556</sup> |||||<sup>557</sup> |||||<sup>558</sup> |||||<sup>559</sup> |||||<sup>560</sup> |||||<sup>561</sup> |||||<sup>562</sup> |||||<sup>563</sup> |||||<sup>564</sup> |||||<sup>565</sup> |||||<sup>566</sup> |||||<sup>567</sup> |||||<sup>568</sup> |||||<sup>569</sup> |||||<sup>570</sup> |||||<sup>571</sup> |||||<sup>572</sup> |||||<sup>573</sup> |||||<sup>574</sup> |||||<sup>575</sup> |||||<sup>576</sup> |||||<sup>577</sup> |||||<sup>57</sup>

Qy 301 GVFPALTAHGTLNVNDVLASCYAVLESHQWAHRAFPALRLHALGALLPGGAVQPTGMHW 360  
 |||||  
 Db 323 GVFPALTAHGTLNVNDVLASCYAVLESHQWAHRAFPALRLHALGALLPGGAVQPTGMHW 382

Qy 361 YSRLLYRLAEELG 374  
| | | | | | | | | : |

Db 383 YSRLLYRLAEELMG 396

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